

CLAIMS

What is claimed is:

1. A method of detecting and/or identifying an agent which binds to mammalian
5 Bonzo or a ligand-binding variant thereof comprising combining:
a) a reference agent that binds mammalian Bonzo,
b) a test agent, and
c) a composition comprising mammalian Bonzo or a ligand-binding variant
10 thereof under conditions suitable for binding of said reference agent to
said Bonzo or ligand-binding variant thereof; and
detecting or measuring the formation of a complex between said
reference agent and said Bonzo or a ligand-binding variant thereof, wherein a
decrease in the formation of said complex relative to a suitable control indicates
15 that said test agent binds to said Bonzo or to a ligand-binding variant thereof,
and wherein said reference agent is not platelet factor-4.
2. The method of Claim 1 wherein said reference agent is a natural ligand for said
Bonzo or a receptor-binding variant thereof.
3. The method of Claim 1 wherein said reference agent is SExCkine or a receptor-
binding variant thereof.
- 20 4. The method of Claim 1 wherein said reference agent is an antibody which binds
to said Bonzo or an antigen-binding fragment thereof.
5. The method of Claim 1 wherein said reference agent comprises a detectable
label.

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6. The method of Claim 5 wherein said label is selected from the group consisting of a radioisotope, an epitope, an affinity label, an enzyme, a fluorescent group and a chemiluminescent group.
7. The method of Claim 1 wherein said composition comprising mammalian Bonzo or ligand-binding variant thereof is a cell that expresses mammalian Bonzo.
8. The method of Claim 7 wherein said cell is a recombinant cell.
9. The method of Claim 7 wherein said cell is a cell line.
10. The method of Claim 1 wherein said composition comprising a functional mammalian Bonzo or ligand-binding variant thereof is a membrane preparation of a cell that expresses mammalian Bonzo or ligand-binding variant thereof.
11. A method of detecting and/or identifying an antagonists of mammalian Bonzo comprising combining:
- a) a cell expressing mammalian Bonzo or a ligand-binding variant thereof;
 - b) a ligand or promoter of said Bonzo; and
 - c) an agent to be tested, under conditions suitable for detecting a ligand- or promoter-induced response; and
- determining the ability of the test compound to inhibit said response, wherein inhibition of a ligand- or promoter-induced response by the agent indicates that the agent is an antagonist, and wherein said ligand or promoter is not platelet factor-4.
12. The method of Claim 11 wherein said cell is a recombinant cell.

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13. The method of Claim 12 wherein said recombinant cell expresses human Bonzo.
14. The method of Claim 11 wherein said ligand or promoter is SExCkine.
15. The method of Claim 11 wherein said response is selected from the group consisting of Ca^{2+} flux, chemotaxis, exocytosis and respiratory burst.
16. A method of detecting a mammalian Bonzo or portion thereof in a biological sample, comprising:
- a) contacting a biological sample with a Bonzo binding agent, under conditions appropriate for binding of said agent to mammalian Bonzo or a portion thereof; and
 - b) detecting binding of said agent thereto;
- wherein the binding of said agent indicates the presence of said Bonzo or portion thereof, and wherein said Bonzo binding agent is not platelet factor-4.
17. The method of Claim 16 wherein the biological sample is of human origin.
18. The method of Claim 16 wherein said binding agent is an antibody which can inhibit the binding of ligand to Bonzo or an antigen-binding fragment thereof.

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19. The method of Claim 18 wherein said antibody or antigen-binding fragment thereof is selected from the group consisting of:
- a) mAb 4A11, mAb 7A2, mAb 7F3;
 - b) an antibody which can compete with mAb 4A11, mAb 7A2 or mAb 7F3 for binding to mammalian Bonzo;
 - c) antigen-binding fragments of (a) or (b) which bind mammalian Bonzo or a portion thereof; and
 - d) combinations of the foregoing.
20. The method of Claim 16 wherein said binding agent is SExCkine or a receptor-binding variant thereof.
21. An antibody or antigen-binding fragment thereof which binds mammalian Bonzo and inhibits the binding of ligand to said Bonzo.
22. The antibody or antigen-binding fragment of Claim 21 wherein said mammalian Bonzo is human Bonzo.
23. The antibody or antigen-binding fragment of Claim 21 wherein said ligand is SExCkine.
24. The antibody or antigen-binding fragment of Claim 21 wherein said antibody or antigen-binding fragment inhibits a cellular response to binding of ligand to said Bonzo in an *in vitro* assay with an IC_{50} of less than about 8 $\mu\text{g/mL}$.
25. The antibody or antigen-binding fragment of Claim 24 wherein said cellular response is selected from the group consisting of Ca^{2+} flux, chemotaxis, exocytosis and respiratory burst.

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26. The antibody or antigen-binding fragment of Claim 24 wherein said cellular response is chemotaxis.

27. The antibody or antigen-binding fragment of Claim 21 wherein the binding of said antibody or said antigen-binding fragment to Bonzo can be inhibited by an antibody selected from the group consisting of mAb 4A11, mAb 7A2 and mAb 7F3.

28. An antibody produced by murine hybridoma 4A11 or an antigen-binding fragment thereof.

29. An antibody produced by murine hybridoma 7A2 or an antigen-binding fragment thereof.

30. An antibody produced by murine hybridoma 7F3 or an antigen-binding fragment thereof.

31. Murine hybridoma 4A11.

32. Murine hybridoma 7A2.

33. Murine hybridoma 7F3.

34. An isolated cell which produces an antibody or antigen-binding fragment thereof that binds to mammalian Bonzo and inhibits the binding of ligand to said Bonzo.

35. The isolated cell of Claim 34 wherein said antibody or antigen-binding fragment inhibits a cellular response to binding of ligand to said Bonzo *in vitro* assay with an IC₅₀ of less than about 8 µg/mL.

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36. The isolated cell of Claim 35 wherein said cellular response is selected from the group consisting of Ca^{2+} flux, chemotaxis, exocytosis and respiratory burst.
37. The isolated cell of Claim 35 wherein said cellular response is chemotaxis.
38. The isolated cell of Claim 34 wherein said mammalian Bonzo is human Bonzo.
39. The isolated cell of Claim 34 wherein said ligand is SExCkine.
40. The isolated cell of Claim 34 wherein said isolated cell is selected from the group consisting of an immortalized B cell, a hybridoma and a recombinant cell comprising one or more exogenous nucleic acid molecules that encode said antibody or antigen-binding fragment thereof.
41. An antibody or antigen-binding fragment thereof which binds mammalian Bonzo expressed on the membrane of a cell and inhibits a cellular response to binding of ligand to said Bonzo.
42. The antibody or antigen-binding fragment of Claim 41 wherein said cellular response is selected from the group consisting of Ca^{2+} flux, chemotaxis, exocytosis and respiratory burst.
43. The antibody or antigen-binding fragment of Claim 42 wherein said antibody or antigen-binding fragment thereof inhibits a cellular response in an *in vitro* assay with an IC_{50} of less than about $8 \mu\text{g/mL}$.
44. The antibody or antigen-binding fragment of Claim 41 wherein said cellular

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response is ~~chemotaxis~~.

45. The antibody or antigen-binding fragment of Claim 21 wherein said mammalian Bonzo is human Bonzo.

5 46. The antibody or antigen-binding fragment of Claim 21 wherein said ligand is SExCkine

47. A method of treating a subject having an inflammatory disease, comprising administering to said subject an effective amount of an antagonist of mammalian Bonzo.

10 48. The method of Claim 47 wherein said antagonist inhibits the binding of ligand to mammalian Bonzo.

49. The method of Claim 48 wherein said ligand is SExCkine.

15 50. The method of Claim 48 wherein said antagonist is an antibody which binds mammalian Bonzo or an antigen-binding fragment thereof.

51. A method of treating a subject having an inflammatory disease, comprising administering to said subject an effective amount of an antibody or antigen-binding fragment thereof which binds mammalian SExCkine and inhibits the binding of said SExCkine to receptor.

20 52. The method of Claim 51 wherein said receptor is Bonzo.

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53. A method of inhibiting a cellular response to binding of ligand to Bonzo expressed on the surface of a leukocyte in a mammal, comprising administering to said mammal an effective amount of an antagonist of Bonzo.
54. The method of Claim 53 wherein said cellular response is selected from the group consisting of Ca^{2+} flux, chemotaxis, exocytosis and respiratory burst.
55. The method of Claim 53 wherein said antagonist inhibits the binding of ligand to Bonzo.
56. The method of Claim 55 wherein said ligand is SExCkine.
57. The method of Claim 55 wherein said antagonist is an antibody which binds Bonzo or an antigen-binding fragment thereof.
58. A method of inhibiting a cellular response to binding of SExCkine to receptor expressed on the surface of a leukocyte in a mammal, comprising administering to said mammal an effective amount of an antibody which binds said SExCkine and inhibits the binding of said SExCkine to receptor.
59. The method of Claim 58 wherein said receptor is Bonzo.
60. A method of modulating a Bonzo function comprising contacting a cell that expresses Bonzo with an agent which binds thereto, thereby modulating the function of said Bonzo.
61. The method of Claim 60 wherein said agent can promote the function of Bonzo.
62. The method of Claim 61 wherein said agent is SExCkine.

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63. The method of Claim 60 wherein said agent can inhibit a function of Bonzo.
64. The method of Claim 63 wherein said agent is an antibody or antigen-binding fragment thereof.
- 5 65. The method of Claim 64 wherein said antibody is selected from the group consisting of mAb 4A11, mAb 7A2 and mAb 7E3.
66. The method of Claim 60 wherein said function is selected from the group consisting of ligand binding, ligand-induced chemotaxis, ligand-induced Ca^{2+} flux, ligand-induced exocytosis and ligand-induced respiratory burst.
- 10 67. A method of recruiting Bonzo⁺ cells to a desired location in a mammal, comprising locally administering to said mammal a therapeutically effective amount of mammalian SExCkine at said location.
68. The method of Claim 67 wherein said desired location is a tumor or a site of infection.
- 15 69. A targeting molecule, comprising a first binding moiety which binds mammalian Bonzo expressed on the surface of a first cell, and a second binding moiety which binds a molecule expressed on the surface of a target cell.
70. The targeting molecule of Claim 69 wherein said first binding moiety is SExCkine or a receptor-binding fragment thereof.

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71. The targeting molecule of Claim 70 wherein said targeting molecule is a fusion protein and the second binding moiety is an antibody or antigen-binding fragment thereof.
- 5 72. The targeting molecule of Claim 71 wherein said antibody or antigen-binding fragment thereof binds a tumor antigen or a viral antigen.
73. The targeting molecule of Claim 69 wherein said first binding moiety is an antibody or antigen-binding fragment thereof.
74. The targeting molecule of Claim 69 wherein said second binding moiety binds a viral or tumor antigen.
- 10 75. The targeting molecule of Claim 73 wherein said second binding moiety is an antibody or antigen-binding fragment thereof.
76. The targeting molecule of Claim 69 wherein said targeting molecule is a bispecific antibody which binds Bonzo and a molecule expressed on a target cell or a bivalent antigen-binding fragment thereof.
- 15 77. A method of effectuating the interaction of a Bonzo⁺ cell with a target cell in a mammal, comprising administering to said mammal an effective amount of a targeting molecule comprising a first moiety which binds mammalian Bonzo, and a second binding moiety which binds a molecule expressed on the surface of said target cell.
- 20 78. The method of Claim 77 wherein said target cell is infected with a virus.
79. The method of Claim 77 wherein said target cell is a tumor cell.

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80. A method of isolating a population of mammalian cells enriched in cytotoxic effector cells, comprising:
- 5 a) contacting a suspension of mammalian cells comprising said cytotoxic effector cells with an antibody or antigen-binding fragment thereof which binds to mammalian Bonzo or a ligand-binding variant thereof under conditions suitable for binding thereto;
- b) separating bound cells from unbound cells; and
- c) recovering the bound cells.
- 10 81. The method of Claim 80 wherein said antibody or antigen-binding fragment is immobilized on a solid support.
82. The method of Claim 80 wherein said antibody or antigen-binding fragment comprises a detectable label.
- 15 83. The method of Claim 82 wherein said detectable label is selected from the group consisting of a magnetic particle, a fluorescent group, an affinity label, a radioisotope, an epitope, an enzyme and a chemiluminescent group.
- 20 84. A test kit for use in detecting the presence of mammalian Bonzo or portion thereof in a biological sample comprising
- a) an agent which binds to mammalian Bonzo or portion of said receptor; and
- b) one or more ancillary reagents suitable for detecting the presence of a complex between said agent and said mammalian Bonzo or a portion thereof, wherein said agent is not platelet factor-4.
85. The test kit of Claim 84 wherein said agent is SExCkine.

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86. The test kit of Claim 84 wherein said agent is an antibody or antigen-binding fragment thereof.

87. The test kit of Claim 86 wherein said antibody inhibits binding of ligand to mammalian Bonzo:

5 88. The test kit of Claim 87 wherein said antibody is selected from the group consisting of

- a) mAb 4A11, mAb 7A2, mAb 7F3;
- b) an antibody which can compete with mAb 4A11, mAb 7A2 or mAb 7F3 for binding to mammalian Bonzo;
- c) antigen-binding fragments of (a) or (b) which bind mammalian Bonzo or a portion thereof; and
- d) combinations of the foregoing.

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89. A test kit for use in detecting the presence of a mammalian SExCkine or portion thereof in a biological sample comprising
- 5 a) at least one antibody or antigen-binding fragment thereof which binds to a mammalian SExCkine or portion thereof, wherein said antibody or antigen-binding fragment thereof inhibits binding of SExCkine to receptor; and
- b) one or more ancillary reagents suitable for detecting the presence of a complex between said antibody or antigen-binding fragment thereof and said mammalian SExCkine or a portion thereof.
- 10 90. An isolated nucleic acid encoding the antibody or antigen-binding fragment of Claim 28.
91. An isolated nucleic acid encoding the antibody or antigen-binding fragment of Claim 29.
92. An isolated nucleic acid encoding the antibody or antigen-binding fragment of Claim 30.
- 15 93. An isolated nucleic acid encoding the targeting molecule of Claim 71.
94. A receptor-binding fragment of SExCkine.
95. The receptor-binding fragment of Claim 94 wherein said fragment binds Bonzo.

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96. The receptor-binding fragment of Claim 94 wherein said fragment has an amino acid sequence consisting essentially of an amino acid sequence selected from:

the sequence of residues 1-200 of SEQ ID NO:3,
the sequence of residues 30-200 of SEQ ID NO:3,
the sequence of residues 1-199 of SEQ ID NO:3,
the sequence of residues 30-199 of SEQ ID NO:3,
the sequence of residues 1-202 of SEQ ID NO:3,
the sequence of residues 30-202 of SEQ ID NO:3,
the sequence of residues 1-155 of SEQ ID NO:3,
the sequence of residues 30-155 of SEQ ID NO:3,
the sequence of residues 1-117 of SEQ ID NO:3,
the sequence of residues 30-117 of SEQ ID NO:3, and
the sequence of residues 30-95 of SEQ ID NO:3.

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